



PATENT

Case Docket No. ACADIA.031A

Date: April 20, 2004

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Weiner, et al.  
Appl. No. : 10/761,787  
Filed : January 21, 2004  
For : USE OF N-  
DESMETHYLCLOZAPINE TO  
TREAT HUMAN  
NEUROPSYCHIATRIC DISEASE  
Examiner : Unknown  
Group Art Unit : Unknown

I hereby certify that this correspondence and all marked attachments are being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on

April 20, 2004

(Date)

Sam K. Tahmassebi, Reg. No. 45,151

TRANSMITTAL LETTER

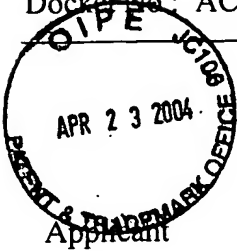
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

Enclosed for filing in the above-identified application are:

- (X) An Information Disclosure Statement.
- (X) A PTO Form 1449 with nineteen (19) references.
- (X) The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment, to Account No. 11-1410.
- (X) Return prepaid postcard.

Sam K. Tahmassebi  
Registration No. 45,151  
Attorney of Record  
Customer No. 20,995  
(619) 235-8550



## INFORMATION DISCLOSURE STATEMENT

Applicant : Weiner, et al.  
App. No. : 10/761,787  
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For : **USE OF N-DESMETHYLCLOZAPINE TO  
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DISEASE**  
Examiner : Unknown  
Group Art Unit : Unknown

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

Enclosed is form PTO-1449 listing 19 references that are also enclosed.

This Information Disclosure Statement is being filed with an RCE or within three months of the filing date of this application and no fee is required in accordance with 37 C.F.R. § 1.97(b)(1), (b)(2), or (b)(4).

Respectfully submitted,  
KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: April 20, 2004

By: Sam K. Tahmassebi

Sam K. Tahmassebi  
Registration No. 45,151  
Attorney of Record  
Customer No. 20,995  
(619) 235-8550

FORM PTO-1449	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO. ACADIA.031A	APPLICATION NO. 10761,787
INFORMATION DISCLOSURE STATEMENT BY APPLICANT  (USE SEVERAL SHEETS IF NECESSARY)		APPLICANT Weiner, et al.	
		FILING DATE January 21, 2004	GROUP Unknown

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE (IF APPROPRIATE)
	1	5,707,798	01/13/98	Brann			

EXAMINER INITIAL	OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PERTINENT PAGES, ETC.)						
	2	Baldessarini, R.J. and Frankenburg, F.R., "Clozapine A Novel Antipsychotic Agent," <i>New Engl. J. Med.</i> , 324(11): 746-754 (1991).					
	3	Baldessarini, R.J., Centorrino, F., Flood, J.G., et al. "Tissue Concentrations of Clozapine and its Metabolites in the Rat," <i>Neuropsychopharmacology</i> 9(2):117-124 (1993).					
	4	Berkeley, J.L., Gomez, J., Wess, J., Hamilton, S.E., Nathanson, N.M. and Levey A.I., "M <sub>1</sub> Muscarinic Acetylcholine Receptors Activate Extracellular Signal-Regulated Kinase In CA1 Pyramidal Neurons In Mouse Hippocampal Slices," <i>Mol. Cell. Neurosci.</i> 18(5): 512-24 (2001).					
	5	Bodick, N.C., Offen, W.W., Levey, A.I., et al "Effects of Xanomeline, a Selective Muscarinic Receptor Agonist, on Cognitive Function and Behavioral Symptoms in Alzheimer's Disease," <i>Arch Neurol.</i> , 54: 465-473 (1997).					
	6	Bondesson, U. and Lindström L.H., "Determination of clozapine and its N-demethylated metabolite in plasma by use of gas chromatography-mass spectrometry with single ion detection," <i>Psychopharmacology</i> 95: 472-475 (1988).					
	7	Brown, J.H. and Taylor, P., "Muscarinic Receptor Agonists and Antagonists," <i>The Pharmacological Basis of Therapeutics</i> , McGraw-Hill, New York, pp 141-160 (1996).					
	8	Centorrino, F., Baldessarini, R.J., Kando, J.C., et al., "Clozapine and Metabolites: Concentrations in Serum and Clinical Findings During Treatment of Chronically Psychotic Patients," <i>J. Clin. Psychopharmacol.</i> 14:119-125 (1994).					
	9	Davis, R.E.; Doyle, P.D.; Carroll, R.T.; Emmerling, M.R.; and Jaen, J., "Cholinergic Therapies for Alzheimer's Disease: Palliative or disease altering?" <i>Arzneimittel-Forschung/Drug Res.</i> , 45(1), 425-431, 1995.					
	10	Eglen, R.M., Choppin, A., and Watson, N., "Therapeutic opportunities from muscarinic receptor research," <i>Trends Pharmacol Sci.</i> 22(8): 409-414, August 2001.					
	11	Hunziker, F, Fisher, E. and Schmutz, J. "11-amino-5H-dibenzo[b,e]-1,4-diazepine," <i>Mitteilung uber siebengliedrige Heterocyclen Helv Chim Acta</i> , 5:1588-1599 (1967).					
	12	Jann, M.W., Grimsley, S.R., Gray, E.C., and Chang, W. "Pharmacokinetic and Pharmacodynamics of Clozapine," <i>Clin. Pharmacokinet.</i> 24(2): 161-176 (1993).					
	13	Jensen, A.A., Spalding, T.A., Burstein E.S., et al. "Functional Importance of the Ala <sup>116</sup> -Pro <sup>136</sup> Region in the Calcium-sensing Receptor, Constitutive Activity and Inverse Agonism in a Family C G-Protein-Coupled Receptor," <i>J. Biol. Chem.</i> 275(38):29547-55 (2000).					
	14	Kuoppamäki, M., Syvälahti, E., and Hietala, J, "Clozapine and N-desmethylozapine are potent 5-HT <sub>1C</sub> receptor antagonists," <i>Eur. J. Pharm.</i> 245:179-182 (1993).					
	15	Moroi, S.E. and Lichter, P.R., "Ocular Pharmacology," <i>The Pharmacological Basis of Therapeutics</i> , McGraw-Hill, New York, pp 1619-1645, (1996).					
	16	Olianas, M.C., Maullu, C., and Onali, P., "Mixed Agonist-Antagonist Properties of Clozapine at Different Human Cloned Muscarinic Receptor Subtypes Expressed in Chinese Hamster Ovary Cells," <i>Neuropsychopharmacology</i> , 2(3): 263-270 (1999).					

EXAMINER

DATE CONSIDERED

\*EXAMINER: INITIAL IF CITATION CONSIDERED, WHETHER OR NOT CITATION IS IN CONFORMANCE WITH MPEP 609; DRAW LINE THROUGH CITATION IF NOT IN CONFORMANCE AND NOT CONSIDERED, INCLUDE COPY OF THIS FORM WITH NEXT COMMUNICATION TO APPLICANT.

FORM PTO-1449	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO. ACADIA.031A	APPLICATION NO. 10/761,787
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		FILING DATE January 21, 2004	GROUP Unknown

EXAMINER INITIAL	OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PERTINENT PAGES, ETC.)	
	17	Weigmann, H., Härtter, S., Fischer, V., Dahmen, N., and Hiemke, C., "Distribution of clozapine and desmethylclozapine between blood and brain in rats," <i>European Neuropharmacology</i> 9: 253-256 (1999).
	18	Weiner, D.M., Burstein, E.S., Nash, N., et al., "5-Hydroxytryptamine <sub>2A</sub> Receptor Inverse Agonists as Antipsychotics," <i>J. Pharmacol. Exp. Ther.</i> , 299(1):268-76 (2001).
	19	Zorn, S.H., Jones, S.B., Ward, K.M., and Liston, D. R., "Clozapine is a potent and selective muscarinic M <sub>4</sub> receptor agonist," <i>Eur. J Pharm.</i> 269: R1-R2 (1994).

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